Claims

1. An isolated and recombinant fusion peptabody, which binds to a member of the epidermal growth factor receptor comprising at least:

(a) a portion of a humanized or human cartilage oligomer matrix polypeptide;

(b) a portion of a hinge and

(c) an epidermal growth factor receptor ligand comprising at least a motif having a three-dimensional structure,

and whereby said isolated and recombinant fusion peptabody is capable of inducing cellular death in a cell expressing epidermal growth factor receptor.

2. The isolated and recombinant fusion peptabody of claim 1, wherein the member of the epidermal growth factor receptor is ErbB1, ErbB3 or ErbB4.

3. The isolated and recombinant fusion peptabody of claim 2, wherein the member of the epidermal growth factor receptor is ErbB1.

4. The isolated and recombinant fusion peptabody of claims 1-3, which is fully human or humanized.

5. The isolated and recombinant fusion peptabody of claims 1-4, wherein said isolated and recombinant fusion peptabody is multimeric.

6. The isolated and recombinant fusion peptabody of claims 1-5, wherein the portion of the hinge is a region of an immunoglobulin polypeptide, which is located at the C terminus of the portion of the humanized cartilage oligomer matrix polypeptide.

7. The isolated and recombinant fusion peptabody of claims 1-6, wherein the epidermal growth factor receptor ligand is located at the C terminus of the portion of the hinge.

8. The isolated and recombinant fusion peptabody of claims 1-7, further comprising an enhancer sequence wherein said enhancer sequence is located at the N terminus of the portion of the humanized cartilage oligomer matrix polypeptide.

9. The isolated and recombinant fusion peptabody of claim 8, wherein the enhancer sequence is selected from the group comprising: YSFE, YSFED, YSFEDL, YSFEDLY, YSFEDLYR and YSFEDLYRR.

10. The isolated and recombinant fusion peptabody of claims 1-9, wherein said epidermal growth factor receptor ligand is selected among the group of:

(a) an epidermal growth factor polypeptide or fragments or variants thereof,
(b) a growth blocking peptide or fragments or variants thereof,
(c) a TGF alpha polypeptide or fragments or variants thereof,
(d) a plasmocyte spreading peptide or fragments or variants thereof,
(e) a paralytic peptide or fragments or variants thereof,
(f) a cardioactive peptide or fragments or variants thereof,
(g) an amphiregulin polypeptide or fragments or variants thereof,
(h) a heparin-binding epidermal growth factor-like polypeptide or fragments or variants thereof,
(i) a betacellulin polypeptide or fragments or variants thereof, or
(j) a viral EGF-like polypeptide or fragments or variants thereof.

11. The isolated and recombinant fusion peptabody of claim 10, wherein said epidermal growth factor receptor ligand is present in its full-length sequences.

12. The isolated and recombinant fusion peptabody of claims 1-11, further comprising a polyhistidine tag sequence.

13. The isolated and recombinant fusion peptabody of claims 1-12, further comprising at least one effector region.

14. The isolated and recombinant fusion peptabody of claim 13, wherein the effector region comprises a cytotoxin.

15. The isolated and recombinant fusion peptabody of claim 13, wherein the effector region comprises a detection moiety.

16. The isolated and recombinant fusion peptabody of claim 15, wherein the said detection moiety is fluorescent.

17. An isolated and purified DNA sequence encoding the isolated and recombinant fusion peptabody of any one of claims 1-13.

18. A vector comprising at least one copy of the isolated and purified DNA sequence of claim 17.

19. The vector of claim 18, further comprising a promoter operably linked to said isolated and purified DNA molecule.

20. A prokaryotic or eukaryotic host cell capable of expressing the isolated and purified DNA molecule of claim 17.

21. A pharmaceutical composition comprising as an active substance a pharmaceutically effective amount of an isolated and recombinant fusion peptabody of claims 1-16 optionally in combination with pharmaceutically acceptable carriers, diluents and adjuvants.

22. Use of the pharmaceutical composition of claim 21, for the preparation of a medicament for the treatment or prevention of cancer.

23. Use according to claim 22, wherein the cancer is selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, liposarcoma, neuroendocrine tumor, mesothelioma, schwanoma, meningioma, adenocarcinoma, melanoma, leukemia, lymphoid malignancy, squamous cell cancer, epithelial squamous cell cancer, lung cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, testicular cancer, esophageal cancer, a tumor of the biliary tract, and head and neck cancer.

24. Use according to claim 23, wherein the cancer is head cancer, neck cancer, bladder cancer or melanoma.

25. A method of treating or preventing cancer that expresses epidermal growth factor receptors selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, liposarcoma, neuroendocrine tumor, mesothelioma, schwanoma, meningioma, adenocarcinoma, melanoma, leukemia, lymphoid malignancy, squamous cell cancer, epithelial squamous cell cancer, lung cancer, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, rectal cancer, colorectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, anal carcinoma, penile carcinoma, testicular cancer, esophagael cancer, a tumor of the biliary tract, and head and neck cancer, comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 21 to a subject.

26. The method of claim 25, wherein the cancer is head cancer, neck cancer, bladder cancer or melanoma.

27. A method for inducing apoptosis and/or necrosis, comprising contacting a cell with the isolated and recombinant fusion peptabody of claims 1-16.

28. The method of claim 27, wherein said cell is a cancer cell.

29. A method for inhibiting cell proliferation, comprising contacting a cell with the isolated and recombinant fusion peptabody of claims 1-16.

30. The method of claim 29, wherein said cell is a cancer cell.

31. A method of diagnosing cancer, comprising administering to a subject the isolated and recombinant fusion peptabody of claims 15-16, optionally in combination with pharmaceutically acceptable carriers, diluents and adjuvants.

32. A kit for treating cancer that expresses epidermal growth factor receptors in a human patient, said kit comprising the isolated and recombinant fusion peptabody of claims 1-16, optionally with reagents and/or instructions for use.

33. The kit of claim 32, further comprising a separate pharmaceutical dosage form comprising an additional anti-cancer agent selected from the group consisting of chemotherapeutic agents, anti-epidermal growth factor receptors antibodies, radioimmunotherapeutic agents, and combinations thereof.

34. A kit for diagnosing cancer that expresses epidermal growth factor receptors in a human patient, said kit comprising the isolated and recombinant fusion peptabody of claims 15-16, optionally with reagents and/or instructions for use.

35. A method for producing the isolated and recombinant fusion peptabody of claims 1-16, comprising the steps of:

a) constructing an isolated and purified DNA molecule encoding the isolated and recombinant fusion peptabody of any one of claims 1-13,

b) allowing expression of said isolated and purified DNA molecule in a cell system under suitable conditions,

c) recovering the isolated and recombinant fusion peptabody.

36. The method of claim 35, characterized in that the cell expression system is a prokaryotic cell.

37. The method of claims 35-36, characterized in that the suitable conditions consist in culturing the cell expression system at a temperature between 10-40 °C during 2-40 hours.

38. The method of claim 37, characterized in that the suitable conditions consist in a temperature of 37°C during 8-16 hours.

39. The method of claims 35 to 38, characterized in that step c) is achieved by extraction of said isolated and recombinant fusion peptabody from the cell expression system subsequently followed by purification and refolding steps.

40. The method of claim 39, characterized in that the purification is carried out in the presence of reducing agents and results in the elimination of contamination.

41. The method of claim 39, characterized in that the refolding step is carried out by direct dilution in refolding buffer and further comprises serial dialysis.

42. The method of claim 41, characterized in that the direct dilution in refolding buffer leads to a final concentration of the isolated and recombinant fusion peptabody below 300 nM.

43. The method of claim 41, characterized in that the serial dialysis comprise at least 2 different dialysis buffers.

44. The method of claim 41, characterized in that the refolding step consists in the oxidation of the isolated and recombinant fusion peptabody before its concentration.

45. A purified and isolated enhancer sequence having protein production increasing activity, characterized in that said purified and isolated enhancer sequence is selected from the group comprising: YSFE, YSFED, YSFEDL, YSFEDLY, YSFEDLYR and YSFEDLYRR, a fragment thereof, a molecular chimera thereof and variants thereof.